

Attorney Docket No.: DRE-0055
Inventors: Laurencin et al.
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braided scaffold.

2. (amended) A replacement construct comprising a degradable polymeric fiber-based, three-dimensional braided scaffold seeded with cells, ingrowth of which is supported by the scaffold.

3. (amended) The replacement construct of claim 2 wherein the cells are mesenchymal in origin.

REMARKS

Claims 1-11 are pending in the instant application. Claims 1-11 have been rejected. Claims 1 2 and 3 have been amended. No new matter has been added by these amendments. Reconsideration is respectfully requested in light of these amendments and the following remarks.

I. Amendments to Specification

In accordance with the Examiner's suggestion, Applicants have amended the specification to capitalize the trademarks LEED-KEIO, DACRON and GORE-TEX. Generic terminology for the trademarks LEED-KEIO and GORE-TEX was already provided in the specification at page 3. With respect to DACRON, Applicants have

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amended the specification at page 3 to provide generic terminology for this trademark as well.

II. Objections to claims

Applicants have amended claims 2 and 3 in accordance with the Examiner's suggestion changing "support" to --supported-- in claim 2 and "where" to --wherein-- in claim 3. Withdrawal of these objections to the claims is respectfully requested in light of these amendments.

III. Rejection of Claims 1 and 6 under 35 U.S.C. § 102(b)

Claims 1 and 6 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Hlavacek et al. (U.S. Patent 4,792,336). The Examiner suggests that Hlavacek et al. discloses a braided ligament or tendon implant with all the elements of claim 1 and a method for replacing damaged ligament by implanting the construct as set forth in claim 6.

Accordingly, in an earnest effort to advance the prosecution of this case and to distinguish the instant invention from the teachings of Hlavacek et al. Applicants have amended claim 1 to clarify that the replacement construct comprises a degradable,

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porous, polymeric fiber-based, three-dimensional braided scaffold. Support for this amendment can be found throughout the specification and in particular at page 9, lines 22-28.

Hlavacek et al. is silent with respect to their fibers being porous. Accordingly, this reference does not teach all the elements of the claimed invention and therefore cannot anticipate the claims as amended. See MPEP §2131.

Withdrawal of this rejection under 35 U.S.C. § 102(b) is therefore respectfully requested.

IV. Rejection of Claims 2-5, 7, and 8-11 under 35 U.S.C. § 103(a)

Claims 2-5 and 7 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Hlavacek et al. in view of Vacanti et al. (U.S. Patent 5,855,610). The Examiner suggests that it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to look to the teachings of Vacanti et al. to modify the ligament or tendon implant of Hlavacek et al. to seed the polymeric scaffold with cells in order for a more rapid development and differentiation process of the tissue being formed and added strength to the scaffold prior

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to implantation.

Claims 8-11 have also been rejected under 35 U.S.C. § 103 as being unpatentable over Vacanti et al. in view of Hlavacek et al. The Examiner suggests that Vacanti et al. discloses a method for producing a graft material composed of living cells in a degradable matrix with all the elements of claim 8, but is silent to the scaffold being braided. However, the Examiner suggests that it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to make the degradable, polymeric fiber-based, three-dimensional scaffold of Vacanti et al. braided in order to impart the desired strength and stiffness in the primary loading direction.

Applicants respectfully traverse these rejections.

In accordance with MPEP § 2143, to establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art must teach or suggest all claim limitations.

As acknowledged by the Examiner, Hlavacek et al. is silent

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with respect to seeding of the matrix with cells.

Further, while Vacanti et al. teaches that their matrix may optionally be seeded with dissociated cells, it is required in the matrix of Vacanti et al. that it first be implanted into a recipient human or animal for a period of time sufficient to form extracellular matrix. The cell-matrix structure is then harvested and used for implantation at the site of injury.

Accordingly, this combination of references provides no reasonable expectation of success that a braided matrix of the present invention merely seeded with cells and not implanted to form extracellular matrix would provide a useful graft material or replacement construct.

*does not
preclude
implanting*

Thus, since this combination of prior art does not meet all the criteria required to render the invention prima facie obvious, it is respectfully requested that these rejections under 35 U.S.C. § 103(a) be withdrawn.

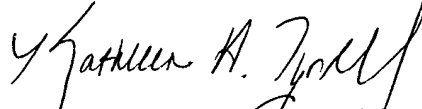
V. Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

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Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "VERSION WITH MARKINGS TO SHOW CHANGES MADE."

Respectfully submitted,



Kathleen A. Tyrrell
Registration No. 38,350

Date: January 2, 2003

Licata & Tyrrell P.C.
66 E. Main Street
Marlton, New Jersey 08053

(856) 810-1515

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

Please replace the paragraph at page 3, lines 1-12 with the following paragraph:

Synthetic ligament grafts or graft supports include carbon fibers, ~~Leed-Keio~~ LEEDS-KEIO ligament (polyethylene terephthalate), the ~~Gore-Tex~~ GORE-TEX prosthesis (polytetrafluoroethylene), the ~~Stryker-Dacron~~ STRYKER-DACRON ligament prosthesis made of ~~Dacron~~ DACRON (condensation polymer obtained from ethylene glycol and terephthalic acid) tapes wrapped in a ~~Dacron~~ DACRON sleeve and the ~~Gore-Tex~~ GORE-TEX ligament augmentation device (LAD) made from polypropylene. These grafts have exhibited good short term results but have encountered clinical difficulties in long term studies. Limitations of these synthetic ligament grafts include stretching of the replacement material, weakened mechanical strength compared to the original structure and fragmentation of the replacement material due to wear.

Please replace the paragraph at page 16, lines 26-34 as follows:

Fibrous scaffolds were fabricated using the 3-D braiding process described in Example 2. Fibers of L-poly lactide (PLA, 70 deniers), polyglycolide (PGA, 60 deniers) and poly-lactide-co-glycolide 82:18 (PLAGA, 70 denier) were laced into 10 fiber/yarn bundles and these yarns were then braided using a 3-D circular braiding machine. Circular 3-D braids of 24 yarns were formed and cut into 1.5 cm lengths for these experiments. ~~Dacron~~ DACRON constructs were similarly formed and used as controls.

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Please replace the paragraph at page 17, lines 8-19 with the following paragraph:

Primary ACL cells were isolated from 1 kg New Zealand white rabbits. The excised ACL was digested using a 0.1% collagenase solution, and only cells collected from fourth digestion were selected for the study. Cells were cultured in α MEM+10% fetal bovine serum, L-glutamine and 1% antibiotics at 37°C and 5% CO₂. ACL cells were seeded on the scaffolds at a density of 80,000 cells/scaffold and grown for up to 28 days. Tissue culture plastic and ~~Dacron~~ DACRON served as control groups. Media were exchanged every two days and for each time point, the pH was measured. Cell growth was measured using the cell-titer 96 assay. Cell morphology and growth on the scaffolds were imaged using SEM.

In the Claims:

Please amend the claims as follows:

1. (amended) A replacement construct comprising a degradable, porous, polymeric fiber-based, three-dimensional braided scaffold.
2. (amended) A replacement construct comprising a degradable polymeric fiber-based, three-dimensional braided scaffold seeded with cells, ingrowth of which is ~~support~~ supported by the scaffold.
3. (amended) The replacement construct of claim 2 ~~where~~ wherein the cells are mesenchymal in origin.